Medica Central Coverage Policy

Policy Name:	**Genetic Testing – Specialty Testing: Respiratory**
Effective Date:	**01/01/2026**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

OVERVIEW

This policy addresses the use of diagnostic tests for disorders that affect the lungs.

For additional information see the Rationale and References section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage. Please see the Concert Platform for additional registered tests.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Alpha-1 Antitrypsin Deficiency			
SERPINA1 Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis	Alpha-1 Antitrypsin (AAT) Mutation Analysis (Quest Diagnostics)	81332, E88.01	Rationale/ References
	SERPINA1 Full Gene Sequencing and	81479, E88.01	

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Deletion/Duplication (Invitae Corporation)		
Cystic Fibrosis			
Diagnostic *CFTR* Sequencing and/or Deletion/Duplication Analysis	Cystic Fibrosis Complete Rare Variant Analysis, Entire Gene Sequence (Quest Diagnostics)	81223, E84.0-9, P09, Q55.4, R94.8, Z13, Z31, Z34, Z82.79, Z83, Z84	Rationale/ References
	Cystic Fibrosis Gene Deletion or Duplication (Quest Diagnostics)	81222, E84.0-9, P09, Q55.4, R94.8, Z13, Z31, Z34, Z82.79, Z83, Z84	
CFTR Intron 9 PolyT and TG Analysis (previously called Intron 8 polyT/TG)	*CFTR* Intron 8 Poly-T Analysis (Quest Diagnostics)	81224, E84.0-9, P09, Q55.4, R94.8, Z13, Z31, Z34, Z82.79, Z83, Z84	Rationale/ References
Other Covered Lung Disorders			
Other Covered Lung Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408	Additional References

RELATED POLICIES

This policy document provides coverage criteria for testing related to respiratory disorders. Please refer to:

- ***Specialty Testing: Multisystem Genetic Conditions*** for coverage criteria related to diagnostic tests for genetic disorders that affect multiple organ systems (e.g., whole exome and genome sequencing, chromosomal microarray, and multigene panels for broad phenotypes).

- ***General Approach to Laboratory Testing*** for coverage criteria related to respiratory testing, including known familial variant testing, that is not specifically discussed in this or another non-general policy.

back to top

COVERAGE CRITERIA

ALPHA-1 ANTITRYPSIN DEFICIENCY

SERPINA1 Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis

I. *SERPINA1* common variant analysis or sequencing and/or deletion/duplication analysis to establish a diagnosis of alpha-1 antitrypsin (AAT) deficiency is considered **medically necessary** when:

   A. The member has any of the following:

1. Chronic obstructive pulmonary disease (COPD), **OR**
2. Unexplained chronic liver disease, **OR**
3. Necrotizing panniculitis, **OR**
4. Granulomatosis with polyangiitis, **OR**
5. Unexplained bronchiectasis, **OR**

B. The member is age 18 years or older, **AND**

1. Has a sibling with a known *SERPINA1* mutation (heterozygous or homozygous).

II. *SERPINA1* common variant analysis or sequencing and/or deletion/duplication analysis to establish a diagnosis of alpha-1 antitrypsin deficiency is considered **investigational** for all other indications.

view rationale

back to top

CYSTIC FIBROSIS

Diagnostic *CFTR* Sequencing and/or Deletion/Duplication Analysis

I. *CFTR* sequencing and/or deletion/duplication analysis to establish or confirm a diagnosis of cystic fibrosis is considered **medically necessary** when:

A. The member has a positive (greater than or equal to 60 mmol/L) or inconclusive (30-59 mmol/L) sweat chloride test, **OR**

B. The member has a positive newborn screen for cystic fibrosis as indicated by elevated immunoreactive trypsinogen, **OR**

C. The member has symptoms of cystic fibrosis from at least **TWO** different organ systems:

1. Sinus (e.g., chronic sinusitis, nasal polyps), **OR**
2. Lower respiratory (e.g., bronchiectasis, chronic or recurrent lower airway infection, allergic bronchopulmonary aspergillosis), **OR**
3. Gastrointestinal (GI)/lumen (e.g., meconium ileus, distal intestinal obstruction syndrome, abnormal motility, rectal prolapse), **OR**
4. Gastrointestinal (GI)/hepatobiliary (e.g., pancreatic insufficiency, recurrent pancreatitis, elevated liver enzymes, ecchymosis, cirrhosis, prolonged neonatal jaundice, fat soluble vitamin deficiencies), **OR**
5. Reproductive (e.g., male (sex assigned at birth) infertility because of obstructive azoospermia, female (sex assigned at birth) infertility), **OR**
6. Other symptoms of cystic fibrosis (e.g., hyponatremic dehydration, failure to thrive, pseudo-Bartter syndrome, aquagenic wrinkling of skin, digital clubbing).

II. *CFTR* sequencing and/or deletion/duplication analysis to establish or confirm a diagnosis of

cystic fibrosis is considered **investigational** for all other indications.

view rationale

back to top

CFTR Intron 9 PolyT and TG Analysis (previously called Intron 8 polyT/TG Analysis)

I. *CFTR* intron 9 polyT and TG analysis in a member is considered **medically necessary** when:

   A. The member has a diagnosis of cystic fibrosis, **AND**

   B. The member has an R117H variant in the *CFTR* gene.

II. *CFTR* intron 9 polyT and TG analysis in a member with a diagnosis of cystic fibrosis is considered **investigational** for all other indications.

view rationale

back to top

OTHER COVERED LUNG DISORDERS

Other Covered Lung Disorders

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

I. Genetic testing to establish or confirm one of the following genetic lung disorders to guide management is considered **medically necessary** when the member demonstrates clinical features[1] consistent with the disorder (the list is not meant to be comprehensive, see II below):

   A. Familial Pulmonary Fibrosis

   B. Primary Ciliary Dyskinesia

   C. Pulmonary alveolar proteinosis (PAP)

II. Genetic testing to establish or confirm the diagnosis of all other lung disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in the *General Approach to Laboratory Testing* (see policy for coverage criteria).

[1]Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference, or other scholarly source.

back to top

RATIONALE AND REFERENCES

SERPINA1 Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis

Alpha-1 Foundation

The Medical and Scientific Advisory Committee published a 2016 clinical practice guideline addressing the diagnosis and management of alpha-1 antitrypsin deficiency (AATD). The guideline recommends that the following be offered testing for AATD: individuals with chronic obstructive pulmonary disease (COPD) regardless of age or ethnicity, individuals with unexplained chronic liver

disease, individuals with necrotizing panniculitis, individuals with granulomatosis with polyangiitis, and individuals with unexplained bronchiectasis (p. 670).

Regarding those with a family history of AATD, the committee recommends that adult siblings of individuals with a known *SERPINA1* mutation be offered testing (p. 673).

Sandhaus RA, Turino G, Brantly ML, et al. The diagnosis and management of Alpha-1 antitrypsin deficiency in the adult. Chronic Obstructive Pulmonary Diseases Journal of the COPD Foundation. 2016;3(3):668-682. doi:10.15326/jcopdf.3.3.2015.0182

back to top

Diagnostic CFTR Sequencing and/or Deletion/Duplication Analysis

Cystic Fibrosis Foundation

Consensus-based guidelines from the Cystic Fibrosis Foundation (2017) outline the ways in which a CF diagnosis can be established. Characteristic features of CF include chronic sinopulmonary disease (such as persistent infection with characteristic CF pathogens, chronic productive cough, bronchiectasis, airway obstruction, nasal polyps, and digital clubbing), gastrointestinal/nutritional abnormalities (including meconium ileus, pancreatic insufficiency, chronic pancreatitis, liver disease, and failure to thrive), salt loss syndromes, and obstructive azoospermia in males (due to congenital absence of the vas deferens, or CAVD).

These guidelines state that, “Individuals presenting with a positive newborn screen, symptoms of CF, or a positive family history, and sweat chloride values in the intermediate range (30- 59 mmol/L) on 2 separate occasions may have CF. They should be considered for extended *CFTR* gene analysis and/ or *CFTR* functional analysis” (p. S8).

Farrell PM, White TB, Ren CL, et al. Diagnosis of Cystic Fibrosis: Consensus Guidelines from the Cystic Fibrosis Foundation [published correction appears in J Pediatr. 2017 May;184:243]. J Pediatr. 2017;181S:S4-S15. e1. doi:10.1016/j.jpeds.2016.09.064

A consensus statement from the Cystic Fibrosis Foundation Consensus Conference authored by Sosnay, et al. (2017) states that an individual with more than one affected organ system has a higher likelihood of having a *CFTR* gene mutation. The statement establishes the following as suspicious symptoms for CF in individuals who may not have received screening for cystic fibrosis, or who may have received a false negative NBS test:

Table II. Clinical signs/symptoms that may signify CF (p. S53)

Presenting conditions	Common as first presentation of CF	Uncommon as first presentation of CF*
Family history	Sibling or parent with CF	Parent of a child diagnosed with CF
Sinus	Chronic sinusitis, nasal polyps	

Lower respiratory	Bronchiectasis, chronic or recurrent lower airway infection (especially *Pseudomonas* infection)	ABPA, nontuberculous mycobacterial infection, asthma, chronic obstructive pulmonary disease
GI/lumen	Meconium ileus, distal intestinal obstruction syndrome	Abnormal motility, rectal prolapse
GI/hepatobiliary	Pancreatic insufficiency, recurrent pancreatitis	Elevated liver enzymes, ecchymosis, cirrhosis, prolonged neonatal jaundice, fat soluble vitamin deficiencies (may present as ecchymosis, anemia, edema, night-blindness, skin rash)
Reproductive	Male infertility because of obstructive azoospermia (CBAVD)	Female infertility
Other	Hyponatremic dehydration,failure to thrive	Pseudo-Bartter syndrome, aquagenic wrinkling of skin, digital clubbing

ABPA, allergic bronchopulmonary aspergillosis; GI, gastrointestinal.

Sosnay PR, White TB, Farrell PM, et al. Diagnosis of Cystic Fibrosis in Nonscreened Populations. The Journal of Pediatrics. 2017;181:S52-S57. e2. doi:10.1016/j.jpeds.2016.09.068

back to top

CFTR Intron 9 PolyT and TG Analysis (previously called Intron 8 poly-T/TG Analysis)

American College of Medical Genetics and Genomics (ACMG)

ACMG has recommended that all R117H positive results require reflex testing for the 5T/7T/9T variant in the polythymidine tract at intron 8 in *CFTR* gene. For R117H/5T positive heterozygotes, testing of parents is recommended to determine the inheritance of the R117H and the 5T variant (i.e., cis vs. trans position). For diagnostic testing, and particularly for testing for CBAVD in males with infertility, it is recommended that the intron 8 variant be included in the testing panel (p. 1294).

Deignan JL, Astbury C, Cutting GR, et al. CFTR variant testing: a technical standard of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2020;22(8):1288-1295. doi:10.1038/s41436-020-0822-5

back to top

ADDITIONAL REFERENCES

1. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/
2. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: https://omim.org/
3. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: https://medlineplus.gov/genetics/.

back to top

Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

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